

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 6 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

REMARKS

Claims 28-38, 55 and 56 are pending. Claim 41 is canceled.

INTERVIEW SUMMARY

Applicants thank Examiners Chong and Padmanabhan for their courtesy extended during the telephonic Interview on February 12, 2007. In the Interview, the patentability of claims 28-38, 41, 55 and 56 was discussed with respect to written description and art cited in the office action. No agreement was reached.

I. CLAIM OBJECTIONS

Objection to claim 41 as being dependent on a canceled claim is rendered moot by cancellation of the claim.

II. REJECTION OF CLAIMS 28-38 and 55-56 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 28-38, 55 and 56 are rejected for lack of written description. The Office Action alleges that there is no support for the limitation "the proanthocyanidin constitutes at least 70 % of an active component of the composition" in claims 28 and 55.

Applicants respectfully submit that the application discloses on page 11, line 19 through page 12, line 17, that the compositions contain one or more proanthocyanidins, each proanthocyanidin present in the composition in a proportion percentage or percentage purity that significantly exceeds a proportion percentage of the same proanthocyanidin's natural presence in a plant, or in an extract from the plant. The application further describes that

In the example of a single PA compound with an excipient to make up the composition, it may be convenient merely to note and compare the percent purity of the compound in the composition, rather than its overall weight percentage, for purposes of the "significantly exceeding" standard, as claimed. In the case of mixtures of PA's it can be appropriate to view a combined percentage composition of the mixed PA's in the therapeutic dosage and compare that figure to a combined percentage presence of the same PA's in the natural plant or extract.

In any event, the purpose of the disclosed standard of measurement is to set forth a fair margin by which a claimed composition exceeds reading on the active ingredients' natural occurrence in plants and conventional extracts of plants.

The specification further states on page 40, lines 24-28 that the proanthocyanidins in the claimed compositions is at least 70% pure proanthocyanidin.

LAI-2849693v1

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 7 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

Therefore, one of skill in the art would recognize that proanthocyanidin is intended to constitute at least 70% of the active ingredient in the instant compositions. Applicants respectfully requests reconsideration and removal of the objection.

**THE REJECTION OF CLAIMS 28-41 and 55-56 UNDER 35 U.S.C. §103(a),
OVER KUZNICKI *ET AL.***

Claims 28-38, 41 and 55-56 are rejected under 35 U.S.C. § 103(a) as being obvious over Kuznicki *et al.* (U.S. Patent No. 5,681,569) because the cited reference allegedly teaches a composition containing green tea solids extracted from tea material. The Office Action states that the extract contains 0.01-0.35% flavanols and catechins, wherein the catechin or a mixture of two or more catechins are catechin, epicatechin, gallic catechin, epigallocatechin gallate and epicatechin gallate, and a pharmaceutical carrier. The Office Action alleges that the green tea composition of Kuznicki *et al.* inherently contains proanthocyanidin oligomers having the instant formula I and II and/or procyanidins such as the dimers and trimers of catechin and epicatechin because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea.

The Office Action further alleges that the inherency of the green tea composition is supported by the Hashimoto *et al.* The Office Action urges that Hashimoto *et al.* teaches that proanthocyanidins are isolated from oolong tea. It is alleged that oolong tea is a well known green tea. The Office Action alleges that the compounds identified by Hashimoto *et al.* in the green tea compositions are the instant compounds having formula I or II.

The Office Action further alleges that Morimoto *et al.* also teaches proanthocyanidin containing compositions wherein the proanthocyanidins can be degraded to catechins and epicatechins.

Applicants note that claim 41 is canceled herein. The rejection is respectfully traversed with respect to pending claims 28-38 and 55-56.

Teaching of Kuznicki *et al.*

Kuznicki *et al.* teaches a liquid composition containing flavanols from green tea extract, sodium and potassium ions, carbohydrate and water. The reference also teaches a dry composition containing flavanols from green tea extract, sodium and potassium ions, carbohydrate (column 2, lines 12-32). The reference further teaches that the term flavanol or

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 8 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

catechin means primarily catechin, epicatechins, and their derivatives (column 3, lines 20-21). The reference describes that the derivatives include sugar, salts, sugar esters, and other edible physiologically available derivatives. It is further described in the reference that the flavanols used therein can be extracted from fruits, vegetables, green tea or other natural sources (column 4, lines 9-11). The reference describes that the drinkable beverage contains about 0.01% to 0.035% **unoxidized, unpolymerized flavanols**.

**Differences between the claimed subject matter and teaching of
Kuznicki *et al.***

Applicants note that the instant claims are directed to a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin as described in the claims and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition.

Applicants have previously argued that there is no literature that indicates the presence of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II in green tea. Applicants provided several references (with the response dated October 14, 2004) that record various components of green tea, such as catechin, epicatechin, gallic catechin, epigallocatechin, epicatechin gallate, epigallocatechin gallate. Furthermore, the cited reference by Kuznicki *et al.* teaches that the components of green tea are catechin, epicatechin, gallic catechin, epigallocatechin, epicatechin gallate, epigallocatechin gallate. The reference also teaches that the drinkable beverage described therein contains 0.01% to about 0.03% **unoxidized, unpolymerized flavanols**. The reference does not teach or suggest that the proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II is present in the green tea extract.

The Office Action does not provide any evidence that the proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II is present in the green tea extract. However, even assuming *arguendo*, that the green tea contains proanthocyanidins of the instant composition, there is no teaching in the reference that the

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 9 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

proanthocyanidin constitutes at least 70% of an active component in the drinkable beverage disclosed therein. As discussed above, the reference teaches that the drinkable beverage disclosed therein contains 0.01% to about 0.03% **unoxidized, unpolymerized flavanols**. It further teaches that the beverage contains caffeine. Kuznicki *et al.* does not teach or suggest that the proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II is present in the beverage. It further does not teach or suggest that proanthocyanidin constitutes at least 70% of an active component in the drinkable beverage. Thus, the cited reference does not teach or suggest the claimed composition.

Teaching of Hashimoto *et al.* and Morimoto *et al.*

The Office Action supports the allegation of inherency based on the teachings Hashimoto *et al.* and Morimoto *et al.* The Office Action alleges that the oolong tea composition taught in Hashimoto *et al.* inherently comprises the instant compounds because these compounds are known to be isolated from oolong tea. It is further alleged that Morimoto *et al.* teaches proanthocyanidins or procyanidins wherein proanthocyanidins can be degraded to catechins and epicatechins.

Applicants submit that Hashimoto *et al.* teaches components of oolong tea extract in 80% aqueous acetone. The reference describes that the 80% aqueous acetone extract of oolong tea contains flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins. Morimoto *et al.* teaches components of *Illicium anisatum* extract in 80% aqueous acetone. The reference teaches that the 80% aqueous acetone extract of *Illicium anisatum* contains several procyanidins, including compounds of formula I and II. The fact that Morimoto *et al.* teaches that the proanthocyanidins can be degraded to catechins and epicatechins is irrelevant to the claimed compositions. Neither of the reference teaches or suggests components of green tea extract described in Kuznicki *et al.*.

The combination of teachings of Kuznicki *et al.* with the teachings of Hashimoto *et al.* and Morimoto *et al.* does not result in the instantly claimed compositions.

The established standard for a *prima facie* showing of obviousness requires the Examiner to show that: (1) the prior art would have suggested to those of ordinary skill in the art that they should make the claimed compositions; and (2) that those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438 (Fed.

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 10 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

Cir. 1991). The primary reference by Kuznicki *et al.* does not teach or suggest that the drinkable beverage taught therein contains proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, wherein proanthocyanidin constitutes at least 70% of the active component as claimed in the instant pharmaceutical compositions. Further, the secondary references by Hashimoto *et al.* and Morimoto *et al.* do overcome this deficiency. The secondary references teach plant extracts in 80% acetone.

Therefore, one of ordinary skill in the art would not be motivated to prepare a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin as described in the claimed compositions and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition. The combined teachings of the cited references do not provide a reasonable expectation of success to prepare such compositions.

The Examiner has the burden of establishing a *prima facie* case of obviousness by showing that the combined prior art references would have suggested the claimed subject matter to one skilled in the art. *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). This burden has not been met by the Office Action.

Because the Office Action fails to satisfy the burden of showing that the cited references suggests or provides motivation to make the instant pharmaceutical compositions, the finding of *prima facie* obviousness is improper. Applicants respectfully submit that a *prima facie* case of obviousness has not been demonstrated and respectfully requests that the rejection under 35 U.S.C. § 103 (a) be reconsidered and withdrawn.

THE REJECTION OF CLAIMS 28, 31-38, 41 and 55-56 UNDER 35 U.S.C. §103(a) OVER JP 10245342

Claims 28, 31-38, 41 and 55-56 are rejected under 35 U.S.C. § 103(a) as being obvious over JP 10245342 because the reference allegedly teaches a pharmaceutical composition for diminishing the toxicity in nerve cells caused by β -amyloid protein containing a catechin or two or more of catechin such as epigallocatechin gallate and epicatechin gallate prescribed in effective amounts for diminishing the toxicity of β -amyloid protein, and a pharmaceutical carrier. The Office Action alleges that the green tea composition disclosed in the cited reference

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 11 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

inherently contains proanthocyanidins oligomers having formula I and II and/or procyanidins such as the dimers and trimers of catechin and epicatechin because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea.

The rejection is respectfully traversed with respect to pending claims 28, 31-38 and 55-56.

Teaching of JP 10245342

JP 10245342 teaches that green tea extract contains polyphenols such as tea catechin and/or theaflavin. The reference teaches composition containing tea catechins and/or theaflavin that can be used for diminishing the toxicity in nerve cells caused by β -amyloid protein. The reference does not teach or suggest a composition containing proanthocyanidins as described in the instant claims.

Differences between the claimed subject matter and the teaching of JP 10245342

The compositions taught in JP 10245342 do not contain proanthocyanidins as described in the instant claims. The reference teaches that the compositions contain tea catechin and/or theaflavin extracted from green tea. As discussed above, there are no references of record to indicate that green tea extract contains a proanthocyanidin selected from the compounds of formula I or II or the oligomeric combinations thereof. Further, there is no teaching in the reference that the proanthocyanidin constitutes at least 70% of an active component in the green tea composition described therein.

Thus, the cited reference does not teach or suggest the claimed composition. Therefore, one of ordinary skill in the art would not be motivated to prepare the pharmaceutical compositions containing a therapeutically effective amount of proanthocyanidins as described in the instant claims and a pharmaceutically acceptable carrier, excipient or diluent. Because the Office Action fails to satisfy the burden of showing that the cited reference suggests or provides motivation to make the instant pharmaceutical compositions, the finding of *prima facie* obviousness is improper. Applicants respectfully submit that a *prima facie* case of obviousness has not been demonstrated and respectfully requests that the rejection under 35 U.S.C. § 103 (a) be reconsidered and withdrawn.

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 12 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

**THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. § 103(a)
OVER HASHIMOTO *ET AL.***

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 103(a) as being obvious over Hashimoto *et al.* because Hashimoto *et al.* allegedly teaches a composition containing or inherently containing a catechin or two or more of catechins such as epigallocatechin and dimers or proanthocyanidins oligomers having the formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin in effective amounts and a pharmaceutical carrier. The Office Action urges that the oolong tea composition in Hashimoto *et al.* inherently comprises the instant compounds because these compounds are known to be isolated from oolong tea. The rejection is respectfully traversed.

**Differences between the claimed subject matter and the disclosure of
Hashimoto *et al.***

Hashimoto *et al.* describes an oolong tea extract in 80% aqueous acetone containing polyphenolic constituents including proanthocyanidins. It does not teach or suggest a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin, as described in the instant claims and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition, and the therapeutic amount of the proanthocyanidin is selected for efficacy in treating amyloid, α -synuclein or NAC fibrillogenesis in a mammalian subject.

The instantly claimed pharmaceutical compositions contain a therapeutically effective amount of a proanthocyanidin and a pharmaceutically acceptable carrier. As well known in the art, 80% aqueous acetone described in the reference is not a pharmaceutically acceptable carrier. The reference does not teach or suggest a pharmaceutically acceptable carrier, diluent, or excipient, as required in the instantly claimed compositions.

Thus, the cited reference does not teach or suggest the claimed composition. Therefore, one of ordinary skill in the art would not be motivated to prepare the pharmaceutical compositions containing a therapeutically effective amount of proanthocyanidins as described in the instant claims and a pharmaceutically acceptable carrier, excipient or diluent. Because the Office Action fails to satisfy the burden of showing that the cited reference suggests or provides motivation to make the instant pharmaceutical compositions, the finding of *prima facie*

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 13 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

obviousness is improper. Applicants respectfully submit that a *prima facie* case of obviousness has not been demonstrated and respectfully requests that the rejection under 35 U.S.C. § 103 (a) be reconsidered and withdrawn.

Rebuttal to Examiner's Arguments

The Office Action alleges that Hashimoto *et al.* discloses catechins extracted and isolated from teas or other plants. It is urged that the percentage purity therein is known to significantly exceed a proportion percentage of the catechin present in a plant.

Applicants respectfully submit that Hashimoto *et al.* describes components of oolong tea extract in 80% aqueous acetone. The reference further teaches that polyphenolic constituents in the 80% aqueous acetone extract of oolong tea include flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins. The reference does not teach or suggest a pharmaceutical composition containing proanthocyanidins and a **pharmaceutically acceptable carrier** as instantly claimed.

THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. §103(a), OVER MORIMOTO *ET AL.*

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 103(a) as being obvious over Morimoto *et al.* because Morimoto *et al.* allegedly teaches a composition containing a catechin or two or more catechins such as epigallocatechin and dimers and procyanidins in effective amounts and in pharmaceutical carrier. The Office Action urges that the compounds identified by Morimoto *et al.* are allegedly the instant compounds of formula I and II. The rejection is respectfully traversed.

Differences between the claimed subject matter and the disclosure of Morimoto *et al.*

Morimoto *et al.* describes that *Illicium anisatum* extract in 80% aqueous acetone contains several procyanidins, including compounds of formula I and II. It does not teach or suggest a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin as described in the instant claims and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition, and the therapeutic amount of the proanthocyanidin is selected for efficacy in treating amyloid, α -synuclein or NAC fibrillogenesis in a mammalian subject.

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 14 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

Applicants respectfully submit that 80% aqueous acetone is not a pharmaceutically acceptable carrier. The reference does not teach or suggest a pharmaceutically acceptable carrier, diluent, or excipient, as required in the instantly claimed compositions.

Thus, the cited reference does not teach or suggest the claimed composition. Therefore, one of ordinary skill in the art would not be motivated to prepare the pharmaceutical compositions containing a therapeutically effective amount of proanthocyanidins as described in the instant claims and a pharmaceutically acceptable carrier, excipient or diluent. Because the Office Action fails to satisfy the burden of showing that the cited reference suggests or provides motivation to make the instant pharmaceutical compositions, the finding of *prima facie* obviousness is improper. Applicants respectfully submit that a *prima facie* case of obviousness has not been demonstrated and respectfully requests that the rejection under 35 U.S.C. § 103 (a) be reconsidered and withdrawn.

Rebuttal to Examiner's Argument: Compounds identified by Morimoto *et al.* are allegedly the instant compounds of formula I and II

In response to the allegation in the Office Action (*see*, page 10) that the compounds identified by Morimoto *et al.* are the instant compounds of formula I and II, Applicants respectfully submit that the instant claims are directed to a pharmaceutical composition containing the proanthocyanidins as described in the instant claims and a pharmaceutically acceptable carrier. The claims are not directed to compounds of formula I and II. Therefore, presence of the compounds of formula I and II in 80% aqueous acetone extract of *Illicium anisatum* does not render the instantly claimed compositions obvious.

THE REJECTION OF CLAIMS 28, 31-41 and 55-56 UNDER 35 U.S.C. §103(a), OVER HATANO *ET AL.*

Claims 28, 31-41 and 55-56 are rejected under 35 U.S.C. § 103(a) as being obvious over Hatano *et al.* because Hatano *et al.* allegedly teaches a composition for anti-HIV containing or inherently containing a catechin or two or more of catechins such as epigallocatechin and dimers of proanthocyanidins oligomers having the formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin in effective amounts and a pharmaceutical carrier. The Office Action urges that the compositions in the cited reference inherently contains

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 15 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

the instant compounds because these compounds are known to be isolated from *Camellia japonica* plants. The rejection is respectfully traversed.

Differences between the claims and the disclosure of Hatano *et al.*

Hatano *et al.* does not teach or suggest a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin as described in the instant claims and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the proanthocyanidin constitutes at least 70% of an active component of the composition and the therapeutic amount of the proanthocyanidin is selected for efficacy in treating amyloid, α -synuclein or NAC fibrillogenesis in a mammalian subject.

Hatano *et al.* teaches that an extract from leaf of *Camellia japonica* contains complex tannins consisting of monomeric hydrolysable tannin and epicatechin, dimeric hydrolysable tannins and complex tannins composed of a dimeric hydrolysable tannin and epicatechin. The reference does not teach or suggest that the extract contains the proanthocyanidin as described in the instant claims. Neither does the reference teach that proanthocyanidin as described in the instant claims constitute at least 70% of an active component of the leaf extract described therein.

Because the Office Action fails to satisfy the burden of showing that the cited reference suggests or provides motivation to make the instant pharmaceutical compositions, the finding of *prima facie* obviousness is improper. Applicants respectfully submit that a *prima facie* case of obviousness has not been demonstrated and respectfully requests that the rejection under 35 U.S.C. § 103 (a) be reconsidered and withdrawn.

Applicant : Alan D. Snow *et al.*
Serial No. : 10/077,596
Filed : February 15, 2002
Page : Page 16 of 16

Attorney's Docket No.: 017170-0010-999
CAM No.: 712576-999005

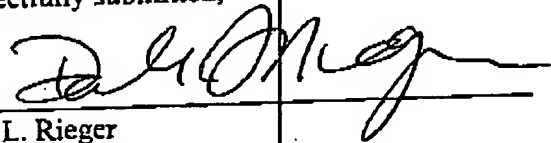
In view of the remarks herein, reconsideration and allowance of the application are respectfully requested.

Applicant hereby petitions under 37 C.F.R. §1.136 for three (3) months extension of time.

Respectfully submitted,

Date: _____

3/14/07



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